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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,945	10/16/2003	Erik Karrer	0241us320	4598

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EXAMINER	
DEJONG, ERIC S	
ART UNIT	**PAPER NUMBER**
1631	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/686,945	KARRER ET AL.	
	Examiner	Art Unit	
	Eric S. DeJong	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *73 and 77-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *73 and 77-81* is/are rejected.

7)☒ Claim(s) *73 and 79* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/01/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Election/Restrictions

Applicant's election without traverse of Group IV (claims 73 and 77-81) in the reply filed on 11/22/2006 is acknowledged.

Information Disclosure Statement

The information disclosure statement filed 11/01/2004 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because it does not list the number of the application in which the information disclosure statement is being submitted, but rather lists the serial number of the earlier filed related application. See 37 CFR § 1.98(a)(1)(i). It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See for example page 80, line 8 and page 91,

line 16. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required:

Claim 80 recites the assays of "half-life extension of a protein pharmaceutical" and "tumorigenesis", however the instant specification does not provide antecedent support for said assays.

Claim 81 recites the desired property of "activation of C1q proteolytic activity", however the instant specification does not provide antecedent support for said property.

Claim Objections

Claims 73 and 79 are objected to because of the following informalities:

Claim 73 recites the limitation "one or more time" in line 11 of said claim and should be amended to read as --one or more times--.

Claim 79 recites the limitation "selecting selecting the at least" in line 1 of said claim and should be amended to read as --selecting the at least--.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 73 and 77-81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 73 recites the limitation "(d) selecting at least one recombinant immunoglobulin constant region nucleic acid encoding a Fc region with a desired property" in lines 9 and 10 of the instant claim. This causes the metes and bounds of the instant claim to be indefinite because it is unclear if the nucleic acid selected in step (d) of the instant claim is limited to one of only to those nucleic acids of the recombinant library produced by step (b) (see lines 5 and 6 of the instant claim), or, alternatively, if the nucleic acid selected in step (d) of the instant claim can be selected from sources other than the recombinant library produced by step (b). Claims 77-81 are also included under this rejection due to their dependence from claim 73.

For the purpose of continuing examination, the limitation "(d) selecting at least one recombinant immunoglobulin constant region nucleic acid encoding a Fc region with a desired property" has been construed to be limited only to selecting at least one recombinant nucleic acid from the recombinant library as set forth in step (b) of the instant claim.

Claim 73 recites the limitation "(e) optionally repeating steps (a) through (d) one or more time until the Fc region has acquired a desired property" in lines 11 and 12 of said claim. This causes the metes and bounds of the instant claim to be indefinite because it is unclear if "a desired property" as recited in step (e) is directed a property of the nucleic acid that encodes a Fc region or, alternatively, is directed to a desired property an Fc region of a protein product generated by a recombinant nucleic acid. It is further unclear from the instant claim if "a desired property" as recited in step (e) is drawn to the same desired property as recited in step (d), or alternatively is drawn to a different desired property. Claims 77-81 are also included under this rejection due to their dependence from claim 73.

For the purpose of continuing examination, the limitation of "a desired property" as recited in step (e) (see line 12 of claim 73) has been construed to be a desired property of the Fc region of a protein product generated from the at least one recombinant nucleic acid as recited in step (d) (see lines 9 and 10 of claim 73). Further, the limitation of "a desired property" as recited in step (e) has been construed to be drawn to a different desired property than the desired property recited in step (d).

Claim 73 is indefinite for reciting an incomplete process that does not include a resolution step that reads back on the preamble of the claimed method. In the instant case, the preamble of claim 73 recites a method for modifying the effector function of an antibody. However, the required process steps are drawn only to providing at least one nucleic acid from at least one immunoglobin heavy chain constant region, recombining

said nucleic acid to produce a recombinant library, and selecting at least one recombinant nucleic acid that has a desired property. The result of practicing the instant claim results in the selection of a recombinant nucleic acid with a desired property. The instant claim does not require that the desired property of said nucleic acid be directed to a modified effector function of an antibody. Claims 77-81 are also included under this rejection due to their dependence from claim 73.

Claim 73 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The instant claim recites process steps drawn only to providing at least one nucleic acid from at least one immunoglobin heavy chain constant region, recombining said nucleic acid to produce a recombinant library, and selecting at least one recombinant nucleic acid that has a desired property. The instant claim omits process steps wherein the at least one recombinant nucleic acid is expressed so as to produce a protein product that has an Fc region. The production of said protein product would be required if the optional processes step (e) (see lines 11 and 12 of the instant claim) was performed so as to determine if an Fc region actually acquired a desired property. Further, said protein product is also required in performing the assays as set forth in dependent claims 78 and 80, as well as for determining the desired properties as set forth in dependent claim 81. Claims 77-81 are also included under this rejection due to their dependence from claim 73.

Claim 77 recites the limitation of "selecting the at least one recombinant immunoglobin constant region nucleic acid *in vitro*" in lines 1 and 2 of said claim. This causes the metes and bounds of the instant claim to be indefinite because it is unclear what process steps are encompasses by selecting a nucleic acid *in vitro*. For example, it is unclear if the "selecting" as recited in the instant claim is intended to further limit the selection step of claim 73, from which claim 77 depends. Further, it is unclear from the instant claim if the "selecting" is alternatively drawn to an actual isolation step of the at least one recombinant immunoglobin constant region nucleic acid from an *in vitro* source, such as an *in vitro* library of recombinant nucleic acids. Further, it is unclear from the instant claim if the "selecting" is alternatively drawn to an *in vitro* assay that characterizes desired properties of the at least one recombinant immunoglobin constant region nucleic acid. Claims 78 is also included under this rejection due to its dependence from claim 77.

Claim 79 recites the limitation of "selecting the at least one recombinant immunoglobin constant region nucleic acid *in vivo*" in lines 1 and 2 of said claim. This causes the metes and bounds of the instant claim to be indefinite because it is unclear what process steps are encompasses by selecting a nucleic acid *in vivo*. For example, it is unclear if the "selecting" as recited in the instant claim is intended to further limit the selection step of claim 73, from which claim 79 depends. Further, it is unclear from the instant claim if the "selecting" is alternatively drawn to an actual isolation step of the at least one recombinant immunoglobin constant region nucleic acid from an *in vivo*

source, such as an *in vivo* library of recombinant nucleic acids. Further, it is unclear from the instant claim if the "selecting" is alternatively drawn to an *in vivo* assay that characterizes desired properties of the at least one recombinant immunoglobin constant region nucleic acid. Claims 80 is also included under this rejection due to its dependence from claim 79.

Claim 81 recites the limitation " the desired property " in line 1 of said claim. There is insufficient antecedent basis for this limitation in the claim because claim 73, from which claim 81 depends, recites "a desired property" in both steps (d) and (e) of said claim. It is unclear which of the two previous recitations of "a desired property" in claim 73, the above limitation is intended to refer.

For the purpose of continuing examination, the limitation " the desired property " in line 1 of claim 81 has been construed to refer only to "a desired property" as recited in step (e) of claim 73.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 73, 77, and 79 are rejected under 35 U.S.C. 102(b) as being anticipated by Daugherty et al.

The instant claims are drawn to a method for modifying the effector function of an antibody comprising the steps of providing at lest one nucleic acid derived from at least one immunoglobulin heavy chain constant region, recombining the at lest one nucleic acid to produce a recombinant library of nucleic acids, and selecting at least one recombinant immunoglobin constant region nucleic acid encoding a Fc region with a desired property.

Daugherty et al. sets forth novel approaches of recombinant PCR technology to graft the complementarity determining regions from a murine monoclonal antibody onto human antibody frameworks (see Daugherty et al., Abstract). Daugherty et al. discloses the engineering of a plurality of chimeric antibodies generated from variable light and heavy chain variable regions of murine origin and constant regions from human sequences, which reads on the claimed steps of providing at least one nucleic acid derived from at least one immunoglobin have chain constant region and recombining the at least one nucleic acid to produce a library as set forth in steps (a) and (b) of claim 73 (see Daugherty et al., page 2471, col. 1, line 17 through col. 2, line 16). The disclosed procedures for expression and assay of recombinant antibodies involved the use of mouse anti-hIgG4 Fc mAb, which demonstrates the present of a Fc region in the chimeric construct and the evaluation of a desired property as set for in step (d) of claim 73 (see Daugherty et al. page 2473, col. 1, line 16 through col. 2, line 12). The disclosed approaches drawn to cloning human variable region templates and transient expression of recombinant human antibody involves both *in vivo* and *in vitro* protocols (see Daugherty et al., page 2471, col. 2, line 18 through page 2473, col. 2, line 12),

which reads on the claimed limitation of selecting at least one recombinant nucleic acid *in vitro* (as recited claim 77) and *in vitro* (as recited in claim 79).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 73 and 77-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Daugherty et al. in view of Ward.

The instant claims are drawn to a method for modifying the effector function of an antibody comprising the steps of providing at lest one nucleic acid derived from at least one immunoglobulin heavy chain constant region, recombining the at lest one nucleic acid to produce a recombinant library of nucleic acids, and selecting at least one

recombinant immunoglobin constant region nucleic acid encoding a Fc region with a desired property. The instant claims are further drawn to embodiments comprising selecting at least one recombinant immunoglobulin constant region of a nucleic acid by performing an assay, as set forth in claims 78 and 80, and selecting a desired property of the Fc region of a recombinant protein product, as set forth in claim 81.

Daugherty et al. sets forth novel approaches of recombinant PCR technology to graft the complementarity determining regions from a murine monoclonal antibody onto human antibody frameworks as discussed above. However, Daugherty et al. does not fairly teach or describe the selection of nucleic acids by use of assays as, set forth in claims 78 and 80, nor the identification of desired properties of an Fc region of a recombinant protein, as set forth in claim 81.

Ward et al. discloses methods and recombinant vectors drawn to immunoglobulin-like domains that include antibody Fc hinge fragments, subfragments, and mutant domains with extended biological half-life (see Ward, Abstract). The disclosure of Ward further includes protein and peptide compositions having altered serum half-lives relative to IgG, methods of making such proteins or peptides, either starting with a known sequence or by screening random sequences, and methods of screening unknown candidate agents for pH dependent Fc receptor binding (see Ward, col. 2, lines 29-52). In addition, Ward discloses methods of making an agent with altered serum half-life by conjugating or otherwise binding of that agent to a moiety identified as having an increased serum half-life through its interaction with Fc receptors, wherein said agents include antibodies, fragments of antibodies, hormones, receptor ligands,

immunotoxins, therapeutic drugs, T-cell receptor binding antigens and other agent that effect increased serum half life (see Ward, col. 2, line 54 through col. 13, line 45).

Therefore it would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to select the recombinant nucleic acids and evaluate the properties of an Fc region of proteins produced by said recombinant nucleic acids, as set forth by Daugherty et al., using the screening methods and assays of Ward because Ward teaches that the disclosed methods are useful for the production of recombinant antibodies or chimeric proteins with improved stability and longevity for therapeutic and diagnostic uses (see Ward, Abstract).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. DeJong whose telephone number is (571) 272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

EDJ EDJ

J.S. Brusca 18 January 2007

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER